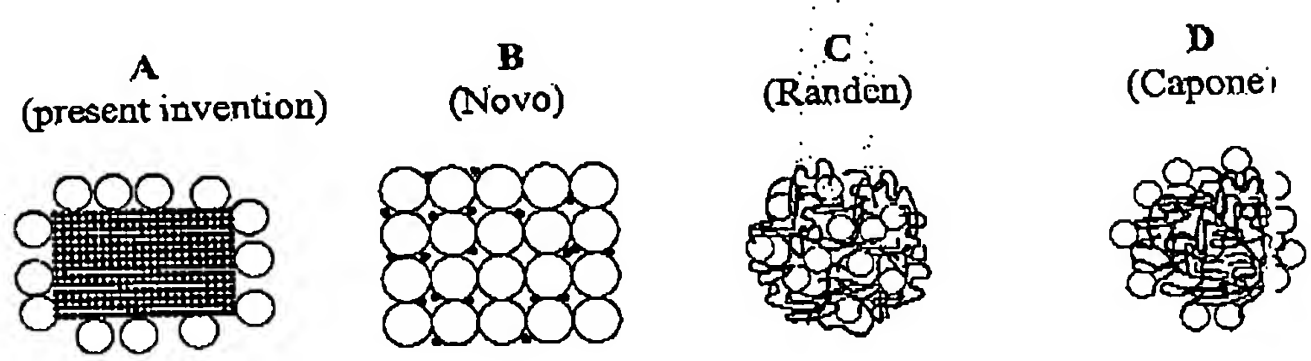
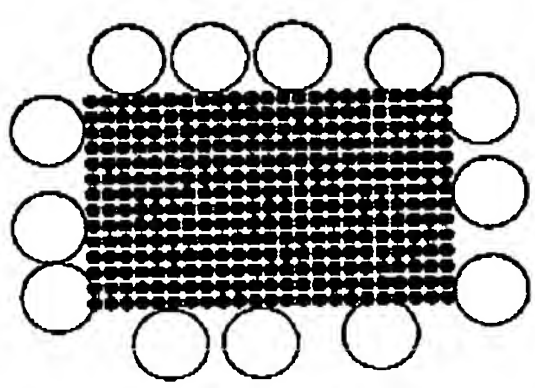
Exhibit I to Amendment dated 01/18/2005

Cross-sections of different types of particles

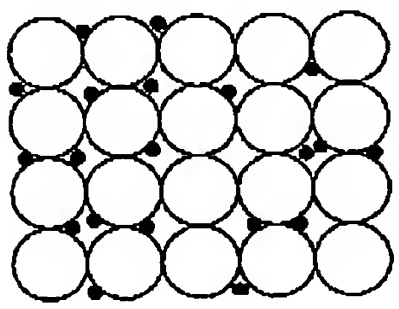


Particle Type A (present invention):



Particles of less than 50 microns with a water soluble coprecipitate core coated with a layer of dehydrated protein. This type of particle can be made using coprecipitates having the properties given in the specification of the present application if the described process is also followed. Use of coprecipitates with preferred properties give rise to a core that is substantially crystalline.

Particle Type B (Novo WO 97/34919):



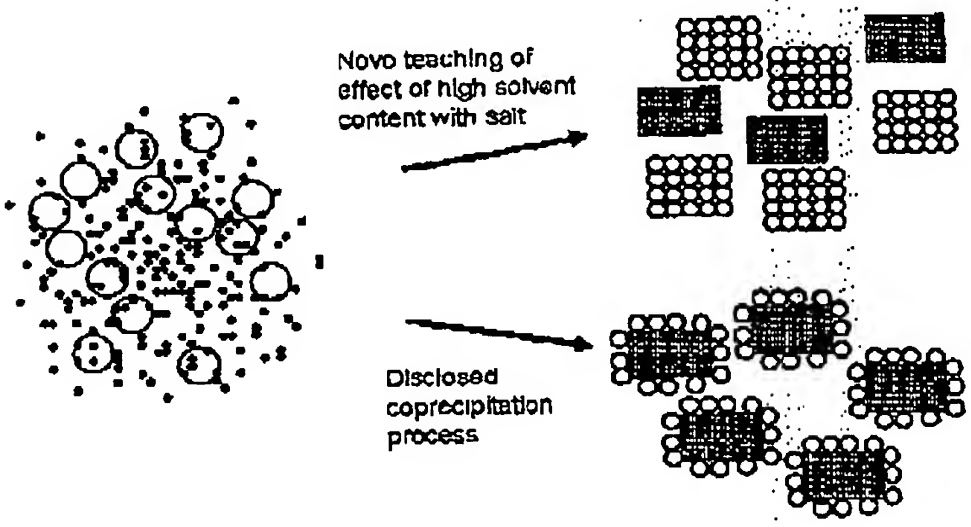
Particle made from an ordered lattice of protein molecules with low levels of salt arising from the crystallisation medium remaining throughout the pores on drying.

The molar ratio of salt:protein in such a particle can be calculated to typically be much less than a 50:1 ratio i.e. assuming a typical wet protein crystal contains 50 wt% solvent which according to Novo WO 97/34919 p15, line 31 will typically contain 0.5-1% w/w salt and taking a protein of Mw 100,000, and the salt to be NaCl (Mw 58.5) the molar ratio is (0.01/58.5) : (1/100000) =

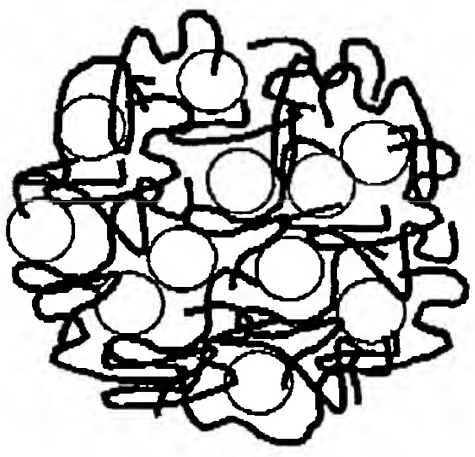
17:1 ratio. Because during the process the aqueous phase containing salt is diluted with solvent the actual value will be less than this.

A further point is that it is well known in the art that drying of protein crystals generally leads to a significant loss of bioactivity. Hence if the Type B particles were to be dried so they contained dehydrated protein it would be significantly inactivated and be unsuitable for many of the applications that Type A particles are useful for, such as biocatalysis.

Novo specifically teaches away from the invention. On page 14 in the paragraph starting on line 14 the use of high solvent content to precipitate more soluble enzymes is discussed. Here it is noted that special precautions need to be taken to avoid contaminating the solid crystalline lipase with solid-phase impurities. To avoid this it is suggested the solvent is added in portions so that separation and subsequent removal of solid-phase impurities by filtration can take place. The skilled person reading this would therefore conclude that addition of excess solvent to a solution containing salt and protein will lead to phase separation of two phases.



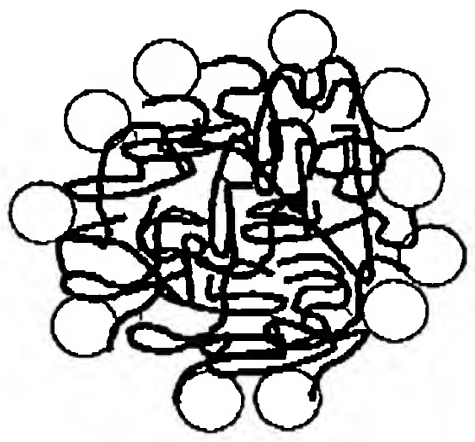
Particle Type C (see Randen):



Particles containing a blend of amorphous carrier (most typically a polymer) and protein. The particles prepared by Randen are an example of Type C. Particles of this kind are typically much larger than Type A particles. In particles of this kind the majority of protein is blended within the interior of the particle and not accessible in the dried state. This makes them unsuitable for

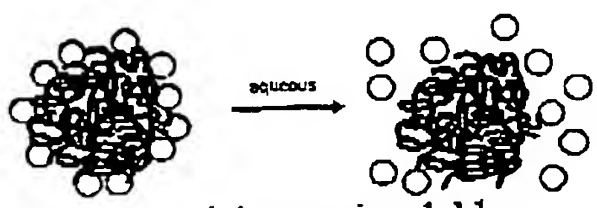
applications such as imaging of biomolecules by probe microscopy or molecular imprinting. On reconstitution, back into aqueous, particles of this type release the protein into solution more slowly that particles of Type A.

Particle Type D (see Capone):

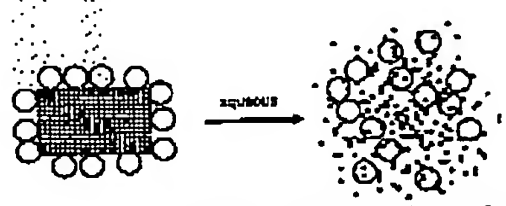


Particles containing a core insoluble in aqueous solution (typically an amorphous polymeric material) onto which a layer of biomolecules can be adsorbed. Preparation of this type of particle is very simple and can be achieved by suspending the core particle in water and adsorbing the protein onto it from solution. This procedure is evidently not possible if the core material is itself water soluble because it will simply dissolve. For Type D particles on resuspension in aqueous a proportion of the protein may be desorbed from the particle but the core remains undissolved. This type of insoluble particle is known to generate an immune response if administered to mammals (see Capone) and is hence unsuitable for many pharmaceutical applications. This type of particle is unsuitable for imprinting into polymers because the core polymer template cannot be removed.

The whole basis of the Capone patent is to prepare particles that can be contacted with cells in an aqueous medium and incorporated into cells in the particulate state by phagocytosis. To the skilled reader it is therefore clear that any particles prepared must be water insoluble or else they would dissolve in the assay medium. Capone describes 2-9 micron particles formed from insoluble polymer beads. Also described are particles of unspecified size formed from Zymosan. The definition of Zyomosan is 'an insoluble largely polysaccharide fraction of yeast cell walls' and it is clear from the preparation procedure described in Example 2 that the Zymosan A used to prepare the particles is water insoluble. On page 3 line 1 it describes preparing the particles by making a suspension of Zymosan in phosphate buffered saline which is then shaken for 1 hour at 37 C. The skilled reader would therefore conclude that it is not possible to prepare water soluble particles by this route.



Type D particle core insoluble



Type A particle core fully soluble